UNIVERSITY OF TASMANIA

Planar Microfluidic Devices and Selective Detection in Gas Chromatography

Techniques and Applications

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A thesis submitted in fulfilment of the requirements for the Degree of Doctor of Philosophy

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Declaration

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1. J. Luong, R. Gras, R.A. Shellie, H.J. Cortes, Applications of planar microfluidic devices and gas chromatography for complex problem solving, ***J. Sep. Sci***. 36 (2013) 182-191.

2. J. Luong, R. Gras, H.J. Cortes, R.A. Shellie, Multi-dimensional gas chromatography with a planar microfluidic device for the characterization of volatile oxygenated organic compounds, ***J. Chromatogr. A*** 1255 (2012) 216-220.

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15. J. Luong, R.A. Shellie, H. J. Cortes, R. Gras, T. Hayward, Ultra-trace level analysis of morpholine, cyclohexylamine, and diethylaminoethanol in steam condensate by gas chromatography with multi-mode inlet, and flame ionization detection, ***J. Chromatogr. A*** 1229 (2012) 223-229.

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Abstract

This graduate research work addresses current techniques and method developments in gas chromatography. The two major themes of the work are to enhance the chromatographic performance and reliability of contemporary capillary column chromatography with the use of planar microfluidic devices, and to garner the power rendered by selective detectors such as micromachined differential ion mobility detection for the improvement of chromatographic aspects related to the portability, selectivity, sensitivity, and throughput of analytical systems. Included in this work are innovative analytical methods developed and successfully implemented to address difficult, unmet, and unarticulated chromatographic needs that have been encountered by the community of practice, particularly in the petrochemical and chemical industries.

Over the course of the development of gas chromatography as a technique, many useful analytical approaches were developed to take advantage of the availability of hundreds of packing materials employed as stationary phases. However, the tools and devices designed for the use in column connectivity for the packed column era are not purposely meant for contemporary capillary column technology. Unfortunately, reliable options are few and far between. Recent advances in metallurgy, metal injection molding, deactivation chemistry, laser etching, and diffusion bonding techniques have resulted in the availability of planar microfluidic devices with features such as built-in fluidic gates, leak-free durability, improved inertness, in-oven and non-contact switching. Therefore, planar microfluidics becomes an important area of research in chromatography. In this work, the important tactical and strategic use of the aforementioned devices in capillary gas chromatography was realized with multiple chromatographic system configurations developed. The use of the device(s) for multi-

dimensional gas chromatography, for hyphenated techniques, epitomized by a unified 1D/2D analytical configuration and two-dimensional gas chromatography – mass spectrometry were attained.

When properly applied, selective detection can substantially ease the burden of separation traditionally imposed on the analytical column especially when the matrices of the samples are increasingly complex to tackle. Selective detection is an enabler to high-speed gas chromatography which is a key component in the development of portable and hand-held analytical devices. Therefore, research conducted in this field is not only important but critical to the capability of and sustainable development for gas chromatography as a technique. In the current research, the performance, benefit, and impact of using differential ion mobility spectrometry with resistively heated temperature programmable micromachined gas chromatography is investigated and its usefulness highlighted. The synergy of hyphenated techniques with other contemporary selective detectors such as the pulsed sulfur chemiluminescence detector and mass spectrometry detector operating in selected ion monitoring mode are also reaffirmed and illustrated in challenging industrial applications.

1. Introduction

1.1 Background

It is difficult to envision a modern organic chemistry laboratory without a gas chromatograph because gas chromatography (GC) is one of the most utilized techniques in analytical chemistry [1-5]. GC has been found to be an analytical solution in many segments; from determining the residues of pesticides in food produce in order to protect the human population, to tracking the airborne chemicals in the battlefields to protect the lives of soldiers and civilians [4-10]. Some of the reasons for GC to be entrusted with such a vital role in analytical chemistry are that GC can be employed for use with analytes ranging from 2 to over 1,000 Daltons. It is relatively low-cost to implement, it is highly dependable, and simple to operate and maintain. In general, as a technique, GC is forgiving; even practitioners with limited experience can obtain good analytical results [11,12].

Despite more than half-a-century of existence, the role of GC has not diminished or been replaced, but the use of GC increases with continual developments in hardware and techniques to tackle a steady increase in sample complexity [13,14]. With advances of the capillary column technology, single dimensional GC was used to meet many critical separation requirements. But in many instances, practitioners had to learn to accept the inherent constraints of the technique because of the limited separation capability it can deliver. Single dimensional GC is the only simple and practical solution available without invoking more sophisticated approaches like selective detection or hyphenated techniques such as gas chromatography – mass spectrometry (GC-MS). Challenges continue to exist in several areas; for instance, the lack of selectivity rendered by commercially available stationary phases employed in both wall-coated and porous-layer open tubular columns especially when dealing with complex matrices.

Attempts to harness the selectivity from columns that have non-similar selectivities or separation mechanisms in wall-coated or porous-layer open tubular formats using techniques like coupled column chromatography, selective tuning, column effluent splitting, or parallel chromatography have met with limited successes. The main reason is that connectivity devices working well in the packed column era are not really compatible for the use with contemporary capillary column chromatography [15,16]. Press-fit connectors are convenient, but can only serve as a short-term, stop-gap solution [17,18]. Degraded chromatography due to frequent leaks, large void volume, and reactivity are some of the disappointments encountered by users.

Recent developments in metal injection molding, milling, and diffusion-bonding technologies have resulted in a new generation of microfluidic devices that hold promise for the techniques cited to be practiced efficiently with capillary column chromatography. One of the methods to fabricate microfluidic devices involves constructing a series of ultra-thin stainless steel plates with the channels and the desired flow architectures precisely etched into the individual stainless steel plate using laser milling techniques. With these techniques, good dimensional control is achieved in the channels and orifices, down to the 25 μm size which can now be manufactured [19,20]. When the thin stainless steel plates are fused together with a technique such as diffusion bonding, a multi-plate wafer is created. The individual thin plates must be precisely aligned to achieve correct link-up of channels and through holes from plate to plate. This multi-plate concept allows very complex flow systems to be fabricated with minimal void volume to preserve the quality of chromatography obtained. While metal is the ideal medium for an in-oven connecting device, it can be rather active for reactive solutes such as pesticides, acids, and bases. Fortunately, there are many well-established techniques that can deliver effective surface passivation, such as chemical and physical vapour deposition [21-23].

The migration from tube-based flow systems to planar micro channel systems affords the delivery of flexible and innovative chromatographic solutions with key features such as built-in fluidic gates, leak-free durability during extensive thermal cycles, having low thermal mass, as well as the ability for in-oven and non-contact switching. In addition, as stated earlier the most important feature is the great inertness derived from advances in surface deactivation techniques [15,16]. Therefore, planar microfluidics have become an interesting area of research in gas chromatography.

The compelling reasons for practicing multidimensional gas chromatography (MDGC) was well articulated right from the first experiment; more than 50 years ago by *Simmon and Snyder* with the first dimension boiling-point separation of hydrocarbons, and a polarity-based analysis of each of the four hydrocarbon groups in a second separation dimension, in sequential applications with a mechanically intensive valve assembly [24]. However, in the late 60s, Deans achieved a major breakthrough with the introduction of a pneumatically based, non-contact switching approach [25]. The invention of the Deans switch brought about a number of competitive advantages including no moving parts at high-temperature operation. The maximum oven temperature was limited not by the material of the valve rotor, but by the column. As a result, the improved maximum oven temperature significantly extends by at least 100 ^{o}C, thereby, enhancing the overall system analytical capability. The Deans switch also enabled basic MDGC operations such as venting and back-flushing. With MDGC, different selectivities of the column stationary phases can be advantageously exploited to attain separation of the analytes of interest [26-32]. The research work conducted by Deans and co-workers was implemented in commercially available MDGC instruments during the 1980s and 1990s [33]. Other commercially available variants emerged including SGE's multi-dimensional conversion system,

Perkin-Elmer's Deans switch instrument, and Gerstel's Deans switch design to name a few [34-36]. Through further developments by Deans and co-workers, a simple coupled column configuration involving two columns having a mid-point pressure that can be controlled independently was innovated. This simple yet elegant approach was adopted by the community of practice to perform MDGC in contemporary systems [37].

While very popular with packed column technology, MDGC has fallen into neglect and become a somewhat forgotten art with the advent of capillary column technology. As mentioned before, this is partly because the devices used for connections suitable for packed column are not necessarily compatible with capillary column technology, and partly because practitioners opted for a path of least resistance on the quest for separation improvement. Hyphenated techniques such as GC-MS were the preferred route to defeat the analytical challenges encountered as the cost of bench-top mass spectrometers fell within many practitioners' model of affordability. Harness the synergies between MDGC and planar microfluidic devices will improve the capability and performance of gas chromatography as a technique.

Unlike other disciplines in analytical chemistry, GC was blessed with having an abundant number of choices of detectors [38,39]. Amongst the available detectors, selective detectors play an important role. Selective detectors contribute tangibly in the delivery of reliable and effective analytical solutions to the practitioners like the use of sulfur chemiluminescence detector for the monitoring of a wide range of sulfur containing compounds in challenging matrices. When properly applied, selective detection can substantially ease the burden of separation imposed on an analytical column especially when the matrices of the samples are becoming increasingly complex and more difficult to deal with. Using this re-distributed separation strategy; selective detection can be an enabler to high-speed GC where the technique has strong positive impact in

the development of portable and hand-held analytical devices. Furthermore, by design, selective detection offers an improved sensitivity for the targeted compounds which is a highly sought after attribute in contemporary analytical sciences [38-40]. Therefore, research effort conducted in this area is not only important but also critical to the capability of and sustainable development for GC itself.

The use of differential ion mobility spectrometry (DMS) as a selective detector was an evolution of ion mobility spectrometry (IMS) [41-46]. DMS approach to garner the differential mobility effect for ion separation was first described in a patent filed by *Gorshkov* and co-workers at the Siberian Academy of Science in the early 1980s as a means to detect explosives [47]. *Buryakov et al.* reported their findings on the performance of one of the first practical DMS spectrometers [48,49]. In the course of DMS development, the geometry of the separation cell, based on a pair of analytical electrodes, has been divided into two approaches: one using flat planar electrodes and the other curved electrodes. Differential mobility sensors with planar electrodes gained strong momentum in the late 1980s in Russia and subsequently leveraged to New Mexico State University (NMSU) in 1996 [50-52]. In collaboration with NMSU, Charles Stark Draper Laboratory built the first prototype micromachined DMS sensor. This technology has been applied to different fields as well as licensed to instrument developers for ultra-trace targeted compounds analysis [53-56].

In contrast with a conventional time-of-flight ion mobility spectrometer, the DMS uses the non-linear mobility in strong radio frequency electric fields for ion filtering. Selective and sensitive detection of targeted analytes of interest can be achieved by using different transport gases, radio frequencies, and associated compensation voltages. When compared with IMS, DMS offers, from a practical standpoint, a notable advantage in which the spectrometer does not

have a shutter gate. This allows virtually all ions to be introduced into the flight tube. The device has no mechanical moving parts, is able to detect both positive and negative ions simultaneously, and is highly suitable for micromachined fabrication. When interfaced with a resistively heated temperature programmable and portable micromachined gas chromatograph with a standard capillary column, the combined platform can be used to address a number of unmet and unarticulated needs in contemporary GC. One particular need is fast analysis, to deliver near real-time, reliable data with low possibility of false positives for field monitoring of otherwise difficult to handle chemicals such as ethylene oxide and bis(chloromethyl) ether in the manufacturing or process environments, non-sulfur odorants in natural gas, and methyl isocyanate in process streams, to cite a few [46,57,58]. The field-deployable platform with low power of consumption also helps improve the quality of results obtained in samples that no longer need to be transported back to the laboratory for analysis. This advantage also helps to minimize the requirement of sample storage and disposal.

In summary, one can predict with a high degree of certainty that, with the advent of planar microfluidic devices, chromatographic component interconnectivities, the techniques of effluent splitting to various detectors, selectively tuning chromatography, parallel chromatography, and multidimensional gas chromatography will not only be reinvigorated, but also be enhanced significantly in their performances. The current research work proves that amongst other configurations, novel approaches such as unifying 1D/2D chromatographic system and three-dimensional separation techniques benefit from advances in planar microfluidics. The concepts and know-how gained from planar microfluidics will be enshrined in contemporary practices of gas chromatography; and further developments continue to have a positive impact on the future of chromatography. The advent of a highly sensitive and tuneable selective detector such as the

DMS when coupled with resistively heated temperature programmable micromachined GC using conventional capillary columns was demonstrated to be a powerful technique and will catalyze further innovations in the portable and eventually hand-held equipment.

1.2 Scope of Thesis

This work has two major themes. The first theme involves leveraging advances in the field of planar microfluidics to reinvigorate and improve the performance of high resolution capillary gas chromatography where reliable inter-column connectivity is a sine-qua-non to the success of multidimensional gas chromatography (GC-GC), comprehensive two-dimensional GC (GC×GC) and in hyphenated techniques like gas chromatography-mass spectrometry (GC-MS) or multidimensional gas chromatography with mass spectrometry (GC-GC-MS). The successful migration from tube based flow systems to planar micro-channel systems allows the delivery of flexible and innovative chromatographic methodologies to address difficult analytical challenges encountered by the community of practice; for instance the use of GC-GC-MS-SIM with planar microfluidic devices for the characterization of industrial relevant analytes or the increase in system flexibility towards a unified 1D/2D analytical system.

The second theme involves combining a recently introduced micromachined differential ion mobility spectrometer with a resistively-heated temperature programmable and portable micromachined gas chromatograph using conventional columns to address challenging analytical needs. The resistively-heated temperature programmable micromachined gas chromatograph was fabricated in-house and is not a commercially available product [59]. The combination of resistively-heated temperature programmable micromachined gas chromatography with differential ion mobility spectrometry addresses the gaps that current conventional benchtop GC

instrumentation does not adequately fulfill due to the analytical speed, portability, sensitivity/selectivity, and logistic requirements.

In addition, included in the work are new analytical methodologies with innovative approaches like the use of a multi-mode inlet to thermally pre-fractionate an aqueous sample for the characterization of trace level of amine-based anti-corrosion agents in process water and the incorporation of an in-house fabricated large volume gas injection system (LVGIS) described elsewhere by *Luong et al*. to achieve part-per-billion (ppb) level analysis of common volatile organic compounds in industrial environments [60,61]. Moreover, the successful implementation of a novel sample introduction technique innovated earlier by *Luong et al*. led to a system detection limit improvement of up to one order of magnitude for the characterization of ultra-trace level of dimethyl sulfoxide in potable water [62,63]. These methodologies were successfully developed and implemented to address difficult analytical challenges encountered in the chemical and petrochemical industries.

Knowledge gained from the scientific endeavours of incorporating planar microfluidics with multidimensional gas chromatography, with hyphenated techniques, the synergy gleaned from combining differential ion mobility detection with resistively-heated temperature programmable micromachined gas chromatography using conventional capillary columns, and the useful methodologies developed contribute to the ultimate desire of sustaining and accelerating further research in gas chromatography.

List of chapter portions which have been removed due to copyright or proprietary reasons:

Chapter 2. Planar Microfluidics in Gas Chromatography
2.1 Applications of planar microfluidic devices and gas chromatography for complex problem solving

2.2 Multi-dimensional gas chromatography with a planar microfluidic device for
the characterization of volatile oxygenated organic compounds

2.3 Multidimensional gas chromatography using planar microfluidic devices for the characterization of chlorinated degreasers in marine gas oil

2.4 Multidimensional gas chromatography for the characterization of permanent gases and light hydrocarbons in catalytic cracking process

2.5 Multidimensional gas chromatography using microfluidic switching and low thermal mass gas chromatography for the characterization of targeted volatile organic compounds

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3.2 Multidimensional GC using planar microfluidic devices for the characterization of phenolic antioxidants in fuels

3.3 Characterization of phenol and alkyl phenols in organic matrixes with

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3.4 Determination of trace ethylene glycol in industrial solvents and lubricants using phenyl boronic acid derivatization and multidimensional gas chromatography

3.5 Planar microfluidic devices in flow modulated comprehensive two dimensional gas chromatography for challenging petrochemical applications

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inlet, and flame ionization detection

5.2 Direct measurement of part-per-billion levels of dimethyl sulfoxide in water by
gas chromatography with stacked injection and chemiluminescence detection

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2. Planar Microfluidics in Gas Chromatography

2.1 Applications of planar microfluidic devices and gas chromatography for complex problem solving

Chapter 2.1 showcases the development, benefit, and impact of planar microfluidics in gas chromatography. While contemporary inlets and detectors were developed for use with high resolution capillary chromatography, the actual hardware used to perform connections and the implementation of techniques that were once popular with packed columns to extend the capability of gas chromatography such as general column coupling, selective tuning, and multidimensional gas chromatography has not kept pace. Tube based flow systems that used to work well based on connections made inside the oven were found to be obsolete. Large thermal mass fittings caused cold spots for high boiling point solutes. Leaks from ferrules and glass press-fit connectors resulted in unreliable system performance. Adsorptivity encountered with ferrules and seals resulted in degraded peak symmetry and peak broadening within the connecting devices themselves. Recent developments with metal injection molding, micromachining, and diffusion bonding technologies have resulted in the commercialization of a new generation of planar microfluidic devices that hold promise to enable the techniques cited to be practiced in an efficient and reliable manner, further enhancing chromatographic performance. Planar microfluidic systems offer key features such as being leak-free over multiple thermal cycles, containing built-in fluidic gates, having low thermal mass, in-column switching, and a high degree of inertness.

In this chapter, the synergies of recently commercialized planar microfluidic devices combined with the resolving power of capillary columns are demonstrated. Novel platform

configurations involving splitting to different detectors, different columns, parallel chromatography, selective tuning, and multidimensional gas chromatography as well as comprehensive two-dimensional gas chromatography are described and applied to a number of notoriously difficult applications such as ultra-trace sulfur containing compounds, anti-hydrating agents in feedstock, and one single analysis for fixed gases, carbon monoxide, carbon dioxide, and light hydrocarbons.

2.2 Multi-dimensional gas chromatography with a planar microfluidic device for the characterization of volatile oxygenated organic compounds

In ***Chapter 2.2*****,** implemented with a five-port planar micro-fluidic device used as a Deans switch, multidimensional chromatography and the employment of chromatographic columns using dissimilar separation mechanisms like that of a selective wall-coated open tubular (WCOT) column and an ionic sorbent coated porous layer open tubular (PLOT) column have been successfully applied to resolve twelve significant volatile oxygenated compounds in both gas and aqueous matrices. These oxygenated compounds are commonly encountered in industrial manufacturing processes such as the bio-oxidation process for waste industrial water treatment. Successful development and implementation of planar microfluidics with multidimensional gas chromatography addressed a challenging analytical measurement gap since it is difficult to separate these analytes from their respective matrices using only single dimension gas chromatography. A novel in-house fabricated large volume gas injection system (LVGIS) was also employed for sample introduction to advantageously enhance system automation, sensitivity, and precision [60]. By successfully integrating these concepts, in addition to having the capability to separate all twelve components in one single analysis, the following features were realized:

1. Multidimensional gas chromatography with dual retention time capability.

2. The ability to quarantine undesired chromatographic contaminants or matrix components in the first dimension column.

3. Back-flushing to improve overall system cleanliness.

With this technique, a detection limit of 250 ppb_v (*liquid*) was attained for all analytes which is quite respectful. Oxygenated compounds are not as sensitive as their corresponding hydrocarbon homologues by flame ionization detection. A complete analysis can be performed in less than 15 minutes.

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2.3 Multidimensional gas chromatography using planar microfluidic devices for the characterization of chlorinated degreasers in marine gas oil

Introduced in ***Chapter 2.3*** is a practical and reliable analytical technique for the characterization of chlorinated degreasers in marine fuels with a five-port planar microfluidic device employed as a Deans switch for multidimensional chromatography and flame ionization detection. The presence of chlorinated degreasers such as trichloroethylene (CAS 79-01-6) and tetrachloroethylene *(*CAS 127-18-4) in marine fuels can lead to accelerated deterioration of engine seals, fuel pumps, valves, and ultimately to catastrophic engine failures. Chlorinated hydrocarbons are not natural components from petroleum refineries. Their presence in marine fuels can be from a variety of sources ranging from inadvertent cross-contamination of blending fuels with cutter stocks of unregulated quality, cross-contamination with industrial waste streams, or from illegal disposing of chlorinated chemical waste in the fuel involved which has become a prominent issue over the last decade in major commercial seaports.

The use of multidimensional gas chromatography allows the minimization if not elimination of potential chromatographic interferences with a significant enhancement of stationary phase selectivity via the use of columns with different separation mechanisms. With the improved selectivities obtained from the column set employed, a mass spectrometer is not required for the application described, thereby making the technique suitable for deployment in remote laboratories such as at marine terminals or fuel quality control laboratories. The advent of an extra pressure source from the Deans switch allows the back-flushing of heavier undesired fuel matrices, improving sample throughput by at least 30% as well as enhancing the overall chromatographic system cleanliness. A complete analysis of the two targeted chlorinated

compounds in marine gas oil can be conducted expediently in less than 15 minutes with detection limits of less than 250 ppb_v.

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2.4 Multidimensional gas chromatography for the characterization of permanent gases and light hydrocarbons in catalytic cracking process

Chapter 2.4 highlights an innovative flexible, integrated gas chromatographic system that employs a novel gas chromatographic configuration consisting of two three-port planar microfluidic devices in series with each other, having built-in fluidic gates, and a mid-point pressure source. The gas chromatographic system has been successfully developed and implemented for the measurement of oxygen, nitrogen, carbon monoxide, carbon dioxide and light hydrocarbons in one single analysis. These analytes are frequently encountered in critical industrial petrochemical and chemical processes such as catalytic cracking of naphtha or diesel to lighter components used in gasoline. Traditionally, due to the lack of an appropriate stationary phase for the analytes cited, a common chromatographic practice involves the use of a series of multi-port switching valves to selectively transfer the effluent of one column to another, or bypass certain columns at various stages in the analysis to prevent the columns from being contaminated by the analytes in the matrix as in the case of carbon dioxide or water on a molecular sieve stationary phase. Under such a scheme, it is common for a system to have three to five multi-port rotary or slider valves and number columns involved. There are some important limitations with this approach, for example, the requirement of a dedicated gas chromatograph as a custom-built analyzer. The requirement for an additional external oven to house the valve assemblies, and the need for a highly accurate pneumatic system to minimize valve-timing shifts over the course of normal use are further complicating factors.

In contrast, the use of planar microfluidic devices offers intangible advantages such as in-oven switching with no mechanical moving parts, an inert sample flow path, and leak-free operation even with multiple thermal cycles. In this way, necessary features such as selectivity

enhancement, column isolation, column back-flushing, and improved system cleanliness are realized. Unlike the traditional multi-valve configuration approach, with planar microfluidic devices the analytical platform developed is highly flexible and can be converted for use in different applications, such as the characterization of alcohols in hydrocarbons, by merely changing the column set on a short notice.

For the application described, porous-layer open tubular capillary columns were employed for the separation of hydrocarbons followed by flame ionization detection. After separation has occurred, carbon monoxide and carbon dioxide were converted to methane with the use of a nickel-based methanizer for detection with flame ionization. Flow modulated thermal conductivity detection was employed to measure oxygen and nitrogen. Separation of all the target analytes was achieved in one single analysis of less than 12 minutes. Oxygen and nitrogen were found to have detection limits of less than 10 ppm_v. Hydrocarbons of interest were found to have detection limits of less than 100 ppb_v.

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2.5 Multidimensional gas chromatography using microfluidic switching and low thermal mass gas chromatography for the characterization of targeted volatile organic compounds

In ***Chapter 2.5,*** using a five-port planar microfluidic device as a Deans switch for multidimensional gas chromatography, and combining this with resistively-heated low thermal mass technology which offers fast temperature programming rate of up to 1800 ^{o}C/min and rapid cool down, a high throughput analytical approach has been successfully developed and implemented for the accurate measurement of fourteen commonly encountered volatile pollutants in chemical manufacturing and process environments. Unique to this analytical configuration, is the use of selective tuning technology with two wall-coated open tubular columns in the first dimension, while in the second dimension a column based on adsorption chromatography was employed to deliver above- ambient separation and enhanced selectivity for the analytes cited. The analytical throughput was improved by leveraging standard features of multidimensional gas chromatography such as the capability to quarantine contaminants, and chromatographic interferences to protect the analytical column used in the second dimension as well as back-flushing of the heavier compounds to improve analytical throughput. The embedded resistively-heated low thermal mass technology offers independent oven control and high throughput when the time it takes for the data to become available is critical to safeguard the health of the manufacturing personnel and the environment. By successfully combining these concepts, a complete analysis of fourteen targeted volatile pollutants can be conducted in less than 120 s. Apart from methane, which has a detection limit of 0.4 ppm_v, the rest of the compounds were found to have detection limits of less than 0.2 ppm_v. The analytical platform was proven to be quite reliable and successfully field implemented.

3. Multidimensional Chromatography with Selective Detection and Hyphenated Techniques

3.1 Tandem sulfur chemiluminescence and flame ionization detection with planar microfluidic devices for the characterization of sulfur compounds in hydrocarbon matrices

Chapter 3.1 introduces a novel concept of incorporating two planar microfluidics devices, a five-port device for use as a Deans switch in multidimensional gas chromatography, and a four-port device to achieve two independent tasks:

a) Combining the effluents from columns employed in the first dimension and second dimension and

b) Splitting the combined effluents to two different detectors in a novel analytical configuration for the characterization of sulfur containing compounds.

With this highly flexible unified 1D/2D configuration, a wide range of common sulfur compounds can be characterized. These compounds include hydrogen sulfide, carbonyl sulfide, carbon disulfide, alkyl mercaptans, alkyl sulfides and disulfides, thiophene, alkyl thiophenes, alkyl benzothiophenes, dibenzothiophene, alkyl dibenzothiophenes and heavier distribution of sulfur compounds over a wide range of matrices spanning a boiling point range of more than 650 ^{o}C. The detection of sulfur containing compounds in different hydrocarbon matrices from light hydrocarbon feedstock to medium synthetic crude oil feed provides meaningful information to optimize refining processes and demonstrates compliance with petroleum product specifications. In tandem with a sulfur chemiluminescence detector used for the measurement of trace sulfur compounds (which offered enhanced sensitivity, selectivity, and equi-molar response to all sulfur

components) is a flame ionization detector. The flame ionization detector can be advantageously used to establish the boiling point range of the sulfur compounds in various hydrocarbon fractions, thereby delivering an elemental specific simulated distillation capability. A complete analysis can be conducted in less than 25 minutes with a detection limit of less than 50 ppb_v (gas) for the analytes of interest.

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3.2 Multidimensional GC using planar microfluidic devices for the characterization of phenolic antioxidants in fuels

Chapter 3.2 showcases the use of multidimensional chromatography hyphenated to mass spectrometry in selected ion monitoring mode for the characterization of hindered phenolic compounds used as antioxidants in fuel. The auto-oxidation process of transportation fuels such as jet fuel, gasoline, and diesel can lead to the formation of deleterious products such as filterable sediments, adherent gums, and polymeric sludge. These undesired by-products can clog filters, fuel lines, fuel injectors, and ultimately cause critical engine failures. To preserve the quality of fuel produced and to enhance fuel storage performance, sterically hindered phenolic compounds are added as antioxidants.

With the incorporation of a five-port planar microfluidic device for Deans switching, a multidimensional gas chromatographic technique has been successfully developed and implemented for the characterization of prominent aforementioned compounds used in fuels such as *2-tert-butylphenol, 2,6-di-tert-butylphenol, 2,6-di-tert-butyl-4-hydroxytoluene,* and *2,4,6-tri-tert-butylphenol*. Detection and quantification of the analytes of interest were conducted with a mass spectrometer in selected ion monitoring (SIM) mode. A complete analysis can be conducted in less than 15 minutes with a detection limit of 50 ppb_w or better.

In addition to the measurement capability described, the use of a single mass spectrometer capable of selectively monitoring the column effluents from either dimension in the context of a unified 1D/2D chromatographic system is an unique analytical configuration. This was accomplished by incorporating into the analytical system a high temperature rotary valve and a 3-port planar microfluidic device. In this way, apart from the intended task of measuring

the analytes cited in selected ion monitoring mode, high molecular weight (C_{25}-C_{40}) fuel contaminants such as engine lube oil, mineral oil or sludge eluting from the first column can also be selectively sent to the mass spectrometer for structural elucidation in SCAN mode. Traditionally, these compounds would have been irreversibly retained in the main analytical column employed in the second dimension.

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3.3 Characterization of phenol and alkyl phenols in organic matrixes with monoethylene glycol extraction and multidimensional gas chromatography/mass spectrometry

In ***Chapter 3.3****,* leveraging the analytical hardware described in *Chapter 3.2*, a new analytical approach has been successfully innovated and implemented for the characterization of phenols and alkyl phenols in organic matrices. Phenol, cresols, and xylenols are chemicals with wide range of applications in the pharmacological and chemical industries. These compounds are found to exist as by-products in coal gasification, Fischer-Tropsch process, crude petroleum oil, petroleum distillate as well as in intermediate process streams in the production of phenol from cumene. The technology developed employs an innovative single-step extraction of the analytes with monoethylene glycol and sonication, followed by multidimensional gas chromatography with mass spectrometry in selected ion monitoring mode for the detection and quantification of the analytes cited. Two planar microfluidic devices involving a five-port and a three-port were employed for the application described. The use of monoethylene glycol as an extraction medium for the application described was found to be unique in analytical chemistry. Ethylene glycol is highly effective in removing phenol, cresols, xylenols, and other alkyl phenols in the matrices described. Extraction efficiency of phenol approached 100% while cresols, xylenols, 4-ethylphenol were 97% or higher, and 2,3,5-trimethylphenol was better than 91% under the analytical conditions used. With the technique described, a complete analysis can be conducted in less than 16 minutes. A practical detection limit of 50 ppb_w was attained for the compounds tested.

3.4 Determination of trace ethylene glycol in industrial solvents and lubricants using phenyl boronic acid derivatization and multidimensional gas chromatography

Chapter 3.4 introduces a novel gas chromatographic approach for the characterization of ppb levels of ethylene glycol in industrial solvents and lubricants. This measurement requirement is known to be very difficult to handle with currently available analytical techniques. Ethylene glycol is a chemical of industrial significance. The major industrial use of ethylene glycol is as a medium for convective heat transfer in, for example, internal combustion engines, HVAC chillers, and solar water heaters. A small leak of glycol in the heat exchange process can have negative consequences, especially with internal combustion engines. This analytical approach can also be employed for the determination of trace ethylene glycol in other matrices. The analytical approach employed a single step derivatization technique that effectively converts ethylene glycol to a cyclic boronate ester, namely 2-phenyl-1,3,2-dioxaborolane, with phenyl boronic acid as a derivatizing reagent. The separation of the derivatized product was enhanced with the use of multidimensional gas chromatography enabled with a five-port planar microfluidic device. The heavy lubricant matrices, like engine crankcase oil, were back-flushed to improve sample throughput and system cleanliness. Detection and quantification of 2-phenyl-1,3,2-dioxaborolane were conducted with mass spectrometry in selected ion monitoring mode. Using the analytical approach described, a complete analysis can be conducted in less than 10 minutes. The analyte of interest was found to have a detection limit of 50 ppb_w.

It was found that propylene glycol can also be analyzed using the same approach. Water does not appear to inhibit the formation of the derivatives, most probably owing to the use of

2,2-dimethoxypropane as a solvent for the derivatizing agent. As a result, this analytical approach may also be useful for the analysis of glycols in an aqueous medium.

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3.5 Planar microfluidic devices in flow modulated comprehensive two dimensional gas chromatography for challenging petrochemical applications

In ***Chapter 3.5*** the utility of planar microfluidic devices and their impact on inter-column connectivity is introduced. In this chapter, two three-port planar microfluidic devices were successfully configured for use as a flow modulator as described by Seeley *et al*. to perform flow modulated comprehensive two-dimensional gas chromatography [22]. A low thermal mass module was also employed to provide independent oven control for each column dimension for the analytical system described.

The utility of the analytical system was demonstrated with a number of challenging petrochemical applications with analytes that possess a wide range of boiling points; from natural gas to crude oil. A variety of columns with different selectivities and separation mechanisms in the categories of porous-layer open tubular (PLOT) and wall-coated open tubular (WCOT) columns were employed for the applications described.

4. Resistively Heated Temperature Programmable Gas Chromatography - Micromachined Differential Ion Mobility Spectrometry

4.1 Resistively heated temperature programmable silicon micromachined gas chromatography with differential mobility spectrometry

Chapter 4.1 highlights the research conducted in the development of a custom-fabricated resistively-heated temperature programmable micromachined gas chromatograph. The GC incorporates a micro-fabricated electromechanical system based on radio-frequency-modulated ion mobility spectrometry (MEMS-RFIMS), also known as differential ion mobility spectrometry (DMS). DMS is the one of the latest additions to the inventory of detectors for chromatography. In contrast to a conventional time-of-flight ion mobility spectrometer, the DMS uses the non-linear mobility dependence in strong radio-frequency electric fields for ion filtering. Selective and sensitive detection of targeted analytes of interest can be achieved by using different transport gases, radio frequencies, and associated compensation voltages. In addition, the detection of both positive and negative ions depending on the ionization mechanism favourable to the analytes involved is achieved. When compared to a stand-alone GC with a non-spectrometric detector or a stand-alone DMS, GC-DMS as a hyphenated technique offers two competitive advantages; two orthogonal separating methods in a single analytical system and the resolving power of gas chromatography to minimize charge exchange in the ionization chamber of the detector.

In this chapter, a portable, resistively-heated temperature programmable silicon machined gas chromatograph with differential mobility detection is introduced. The performance of the instrument is illustrated with examples of known difficult industrial applications such as ultra-trace analysis of methyl isocyanate (CAS 624-83-9), a chemical made infamous by the Bhopal incident, and the characterization of part-per-billion levels of suspected carcinogens such as acetaldehyde (CAS 75-0-70) and acrylonitrile (CAS 107-13-1).

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4.2 Temperature-programmable resistively heated micromachined gas chromatography and differential mobility spectrometry detection for the determination of non-sulfur odorants in natural gas

Introduced in ***Chapter 4.2*** is a portable, fast gas chromatographic method for the direct measurement of ppb level of sulfur-free odorants in commercially available natural gas. The approach incorporates a custom-fabricated, resistively-heated, temperature-programmable silicon micro-machined gas chromatograph that employs a standard capillary column for the fast separation of methyl acrylate (CAS 96-33-3) and ethyl acrylate (CAS 140-88-5) from the natural gas matrix. The separation approach is hyphenated to a micro-machined differential ion mobility spectrometer to enhance analyte detectability, and the overall selectivity obtained against the matrix described. A complete analysis can be conducted in less than 70 s. Further, these two compounds can be measured accurately in the presence of other common volatile sulfur-based odorants such as alkyl mercaptans and alkyl sulfides. A limit of detection for the target compounds at 50 ppb_v was achieved.

4.3 Temperature programmable low thermal mass silicon micromachined gas chromatography and differential mobility detection for the fast analysis of trace level of ethylene oxide in medical work place atmospheres

In ***Chapter 4.3,*** a portable, fast gas chromatographic method for the direct measurement of ppb level of ethylene oxide (CAS 75-21-8) in medical work place atmospheres is presented. The approach incorporates a custom-fabricated resistively-heated temperature programmable silicon micromachined gas chromatograph that employs a standard capillary column with a micromachined differential ion mobility spectrometer to deliver enhanced targeted analyte detectability as well as improving the overall selectivity obtained for the fast separation of ethylene oxide from airborne organic interferences in active treatment healthcare facilities. Ethylene oxide is a chemical of significance in medical science for its critical role as a highly effective sterilizing agent for heat sensitive surgical instruments. However, ethylene oxide is highly flammable, a suspected human carcinogen, and therefore, requires close monitoring.

With the instrumentation and methodology described, ethylene oxide in the matrix mentioned can be measured directly with a low possibility of false positives and without the need for any sample pre-treatment, such as pre-concentration or derivatization. A detection limit of less than 5 ppb_v for ethylene oxide was achieved. A complete analysis can be conducted in less than 60 s. This can substantially improve sample throughput and shorten the wait time for results to become available for a decision to be taken in the event of a chemical excursion.

The technique was found to be reliable, can be field deployable, and is suitable not only for use to monitor ethylene oxide in active health care environments, but also for veterinary clinics, sterile instrument manufacturing facilities, or wherever ethylene oxide is used.

4.4 Determination of trace bis(chloromethyl) ether in air using miniaturized gas chromatography coupled with differential ion mobility spectrometry

In ***Chapter 4.4,*** the direct measurement of part-per-billion level of bis(chloromethyl) ether with a portable, fast gas chromatographic method based on a custom-fabricated temperature programmable low thermal mass silicon micromachined gas chromatography that employs a standard capillary column with differential ion mobility spectrometry is presented. Bis(chloromethyl) ether has been reported to be a human carcinogen even when present at trace levels. The use of a micromachined differential ion mobility spectrometer for the detection of the analyte cited improves overall system sensitivity and selectivity, while resistively-heated temperature programmable micro-machined gas chromatography provides high throughput with near-real time data. Capable of operation at atmospheric pressure; the analytical system allows fast start up with high sample throughput, suitable for field operation and rapid response in the event of an excursion. With the technique described, bis(chloromethyl) ether can be measured directly without pre-concentration or derivatization with low possibility of false positive results. A complete analysis can be carried out in 60 sec with a detection limit of 2 ppb_v.

Determination of trace bis(chloromethyl) ether in air using differential ion mobility spectrometry coupled with micromachined gas chromatography

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ABSTRACT:

The direct measurement of part-per-billion level of bis(chloromethyl) ether (BCME) using micromachined differential ion mobility spectrometry combined with portable temperature programmable low thermal mass silicon micromachined gas chromatography is described. BCME is a human carcinogen and prominent impurity in the industrial chemical, chloromethyl methyl ether. Unlike chloromethyl methyl ether, which hydrolyzes quickly in air especially in the presence of humidity, BCME is significantly more stable and therefore, can pose a major health hazard to field workers from industrial hygiene and health safety standpoints. With its capability to operate in atmospheric pressure, the analytical system affords fast start up with high sample throughput, and high amenability to field operation and rapid response in the event of an excursion. The technique described can measure bis(chloromethyl) ether directly without pre-concentration or derivatization with low possibility of false positive results. A complete analysis can be carried out in 60 s. A detection limit of 2 uL L^{-1} and relative precision of less than 5% RSD (n = 10) over a range from 5 uL L^{-1} to 500 uL L^{-1} were obtained.

Key words:

Bis(chloromethyl) ether; differential ion mobility spectrometry; gas chromatography; portable GC; low thermal mass gas chromatography.

1. INTRODUCTION

Chloromethyl methyl ether (CMME) is used extensively as an alkylating agent and industrial solvent in the production of membranes, anion exchange resins, dodecylbenzyl chloride, polymers, water repellents, and other aromatic compounds. CMME can typically contain up to 8 per cent of bis(chloromethyl) ether (BCME) as a major impurity [1]. BCME has been classified as a known human carcinogen when present even at low concentration level in air, and has been directly linked to cause lung cancer and tumours in people and animals [2]. While CMME hydrolyzes rapidly in air, especially with humidity, BCME is reportedly stable to at least 18 h even in 70% humidity environment. This poses a potential industrial hygiene and health safety threat to plant personnel. Close monitoring of BCME is required to provide workplace safety and to protect human health.

A number of analytical techniques have been reported for the determination of BCME such as the use of selective tuning gas chromatography, reaction gas chromatography; by reacting BCME with sodium pentachlorophenate, selective detectors including ^{63}Ni based electron capture (ECD), electrolytic conductivity (ELCD) detectors, and high-resolution mass spectrometry [3-7]. To meet the part-per-billion detection limit required, sample enrichment is frequently employed with the use of adsorbents like macrorecticular styrene-divinylbenzene copolymer and 2,6-diphenyl-p-phenylene oxide [3-7]. While the techniques described might be sufficient for passive monitoring of BCME, especially for time weighted average measurements, there are a number of limitations that need to be addressed. First, the delay in data availability can have negative impact on field workers who might continue to be exposed to the chemical in the event of an excursion.

Other limitations include inadequate selectivity against airborne interferences and the lack of field deployable capability for rapid response. While ECD might have sufficient sensitivity for detecting BCME and despite being a selective detector, without adequate chromatographic separation, it can be constrained by interferences from other halogenated, oxygenated, and aromatic compounds found in the manufacturing environment. A portable or benchtop GC-MS operating in selected ion monitoring mode can be used; however, the need for specialized analytical skill to operate and support the instrument, and the overall cost of ownership makes this option less attractive. Further, where sample enrichment approaches are utilised, artifacts arising from adsorbent breakdown caused by multiple thermal desorption cycles, or from BCME reacting with the sorbent and/or other compounds trapped from the matrix can be deleterious to effectiveness of ultra-trace level analysis.

In this investigation, we propose direct measurement of BCME in ambient air at the low part-per-billion level, without enrichment or chemical derivatization, using differential ion mobility spectrometry (DMS) coupled to portable fast gas chromatography. The approach involves coupling a micromachined differential ion mobility spectrometer with a custom-fabricated resistively heated temperature programmable micromachined gas chromatograph. In-depth discussions of DMS technology are reported elsewhere [8-10]. DMS shares many characteristics with ion mobility spectrometry (IMS) yet offers key advantages. Both are designed to operate without a reduced pressure environment. By alleviating vacuum requirements, DMS is suitable for rapid start-up which is a highly sought after attribute for field operation or for emergency response. Unlike IMS however, a moving mechanical shutter gate is not required, so almost all ions produced are introduced into the mass filter. This provides a wider linear range, and does not restrict operation to only positive or negative ion detection.

2. EXPERIMENTAL

Bis(chloromethyl ether) (CAS# 542-88-1) was purchased from Fisher Scientific (Edmonton, Canada). A primary standard of 5 mL L^{-1} BCME in purified laboratory air was prepared. Standards over the range from 5 μL L^{-1} to 500 μL L^{-1} were prepared from the primary standard by serial dilution for calibration purpose with an Environics 2014 Computerized Gas Dilution and Blending System.

Air samples were collected with an inert hand sampling pump and new 200 mL Tedlar bags. All samples were analyzed within the first two hours of sampling to ensure sample integrity had not been comprised. The bags were discarded after use to minimize cross-contamination.

The configuration of the portable analytical system were previously described in Ref [11-13]. Detection of BCME was performed using a micromachined differential ion mobility spectrometer (Sionex, Bedford, USA). Analyte ionization was achieved by using a 185 mbq (5mC) ^{63}Ni ionization source. Detector control and data handling capability were handled by Sionex Expert version 2.5, a software suite provided by the manufacturer. The micromachined differential ion mobility spectrometer temperature was 80 ^{o}C. The radio frequency value (Rf) was 1200V and the compensation voltage value (V_c) was -8.8V. A Hewlett-Packard notebook computer equipped with a Pentium Quad-Core 2.5 Mhz processor, 4 gigabytes of RAM, and 500 gigabyte hard drive with Windows XP Professional SVP-3 as operating system was used to host the software and process the data obtained.

105 An Agilent CP-4900 micromachined gas chromatograph (Agilent Technologies,
106 Middelburg, The Netherlands) was used as the analytical platform. The original isothermal
107 temperature controlled column module was removed and substituted with a locally fabricated
108 temperature-programmable low thermal mass (LTM) column module [14]. The module was
109 equipped with a 10 m × 0.25 mm i.d. × 1 μm trifluoropropyl methyl silicone column, manually
110 coiled to a diameter of 2.54 cm for the separation of BCME. The column was interfaced with a
111 micromachined silicon injector (Agilent Technologies, Middelburg, The Netherlands) *via* the
112 existing inlet interface manifold with seals and compression fittings taken from the standard
113 micromachined isothermal temperature module. The inlet temperature was 120 ^{o}C and an
114 injection time of 250 s was used throughout. Helium carrier gas was supplied at an inlet pressure
115 of 5 psig. Temperature-programming of the low thermal mass column unit was conducted using
116 a standard TC-4 LTM temperature-programming controller (Agilent Technologies, Delaware,
117 USA). The temperature was programmed from 50^{o}C (1 s) to 150^{o}C @ 3.5^{o}C/s, and maintained at
118 150^{o}C for 40 s. On-board pump sampling duration was 30 s and transport gas used was filtered,
119 carbon dioxide free air with a flow rate of 500 mL/min. An Agilent 6890GC (Wilmington,
120 USA) ^{63}Ni electron capture detector (ECD) was also used for detector feasibility study.

121 The outlet of the GC column was connected to a custom, locally fabricated, passivated metal
122 manifold which interfaced to the DMS *via* a heat traced 40 cm × 0.25 mm i.d. deactivated,
123 uncoated fused silica tubing with viton o-rings and compression fittings similar to those used to
124 interface the column inlet to the injector.

125

RESULTS AND DISCUSSION

The DMS used in this work is comprised of two planar electrodes of 15 mm × 1.5 mm separated by a 0.5 mm analytical gap. Ionization is achieved by the use of a 185 mbq (5mC) ^{63}Ni radioactive source. With ^{63}Ni source, $C_2H_4Cl_2O$ (MW 115 Da) will form positive ion species with m/z of 116 $C_2H_4Cl_2OH^+$, 134 $[C_2H_4Cl_2OH(H_2O)]^+$ as well as 152 $[C_2H_4Cl_2OH(H_2O)_2]^+$. $H^+(_nH_2O)$ are metastable positive reactant ions generated from gas phase reaction between the air molecules in the transport gas and beta particles emitted by the ^{63}Ni radioactive source. The following equations describe a simplified scheme for product ion formation for positive ion products in the case of BCME:

$$C_2H_4Cl_2O + H^+(H_2O) \rightarrow C_2H_4Cl_2OH^+ + H_2O$$

The formation of cluster ions can also occur:

$$C_2H_4Cl_2OH^+ + nH_2O \rightarrow C_2H_4Cl_2OH^+.nH_2O$$

Performance optimization for determination of trace level BCME involves finding optimal frequency voltage (V_{Rf}), compensation voltage (V_c), detector temperature, and transport gas flow rate. Amongst these operational parameters, the most critical parameters for the successful performance is selecting an appropriate V_{rf} and corresponding V_c to deliver the best selectivity and sensitivity. Two-dimensional dispersion plots, where both Rf and V_c electronic circuits are synchronized and operated simultaneously, provide analyte information and can be employed to determine optimal regimes of DMS operation for the target analyte. **Figure 1** shows a dispersion plot of outdoor air obtained from a local park on both positive and negative reactant ion product

147 (RIP) channels. RIP background with multiple ion tracks was observed from 500 to 1100 V on
148 the positive channel, and one single ion track was detected from 500 to approximately 1100V on
149 the negative channel. Selecting Rf and V_c values covered by these ion cluster tracks can have a
150 negative impact on both sensitivity and selectivity for the target compound. A dispersion plot of
151 15 mg L^{-1} BCME in purified lab air was shown in **Figure 2**. Apart from the ion tracks from air
152 similar to those seen in Figure 1, a clear and well-formed ion track for BCME was observed on
153 the positive channel. No specific ion track formation for BCME was seen on the negative
154 channel. The preference is to select Rf and V_c values that are on the analyte track and away from
155 the ion tracks produced by the air matrix. Based on the information gleaned from the dispersion
156 plots, an Rf of 1200V with a V_c of -8.8V in the positive channel was selected for this application.
157 A detailed discussion on two-dimensional dispersion plot, topographic plot, the modes of
158 operation of DMS, and strategies in detector optimization have been reported earlier [11, 15, 16].

159

160 The detector used in this work has a maximum operating temperature of 150 ^{o}C mainly because
161 of the materials of construction involved. Previous work showed that the detector should be
162 operated at the lowest temperature possible, but still high enough to avoid the condensation of
163 the matrix or the solute of interest [11]. For the analysis described, a temperature of 80 ^{o}C was
164 selected to maximize the sensitivity and minimize the potential of condensing water moisture in
165 high humidity samples. Transport gas flow rate was found to have a direct positive impact on
166 sensitivity. Purified air was used as transport gas at a flow rate of 500 mL/min.

167

Operating in the continuous selection of target ion mode, the Rf (1200V) and Vc (-8.8V) was held constant to provide centering ion trajectory in the analytical gap of the micromachined DMS. The data obtained are presented as a three dimensional plot, commonly referred to as topographic plot; retention time (y-axis), mobility scan (x-axis), and the ion current intensity (z-axis). With no analyte entering the spectrometer, the DMS spectrum shows only reactant ions associated with transport gas. These are mainly protonated water clusters. When the analyte is eluted from the column, the intensity of the product ion peak increases. This also corresponds with a decrease of the reaction ion peak. Once the analyte is eluted, the product ions peak declines and RIP peak returns back to the original level. The analyte response is displayed as a certain spot, characterized by four distinct parameters with three from the spatial process (spectrometer) and one from the temporal process (GC): the Rf voltage used, the compensation voltage (Vc) on x-axis, the intensitiy of the spot (z-axis), and the retention time (y-axis). As an illustration, **Figure 3** shows a topographic plot of 1 mL L-1 of BCME in purified lab air. A target ion of BCME was detected at Rf of 1200V, V_c of -8.8V, GC retention time of 59 s, with high intensity. No formation of ion cluster was detected in the negative channel. Topographic plots of purified lab air, 50 µL L-1, 1.4 mL L^{-1}, and 7 mL L^{-1} BCME spiked into air obtained from a local industrial area are illustrated in **Figure 4**, demonstrating a high degree of selectivity and sensitivity of the analytical method for BCME.

Silicon micromachined gas chromatography (µGC) separation was introduced to the analytical approach to minimize space cross-charges and to further enhance selectivity. From a form factor standpoint, the DMS is fully compatible with µGC, with each system having low power consumption and inherently low void volume with the micro-fabricated process [17]. A

trifluopropyl methyl silicone stationary phase column was selected to provide enhanced selectivity for BCME from other potential airborne interfering compounds like hydrocarbons and aromatics in exhaust fumes from incomplete combustion of fuels used by internal combustion engines and chlorinated/oxygenated compounds from solvents used at the manufacturing facilities. The short temperature-programming cycle of 50 ^{o}C to 150 ^{o}C was found to be adequate for the removal of any potential higher boiling point compounds that might have accumulated on the column and substantially speed up the analysis when compared to conventional isothermal silicon micromachined gas chromatography.

To conduct accurate measurement, the target measurement mode of the DMS was selected. This feature is akin to selected ion monitoring (SIM) mode in mass spectrometry. Here, the DMS is tuned for the detection of a particular target ion with a fixed parameters including Rf, V_c, temperature, transport gas type and flow rate at a given retention time. The output of the system resembles a regular peak in a chromatogram, which plots intensity versus time. Like in SIM, since the spectrometer does not have to scan across the compensation voltage range from -40 V to +15 V, substantial improvement in sensitivity for the target compound can be realized. **Figure 5** shows chromatograms of 2 and 5 μL L^{-1} BCME spiked into plant air obtained from a local petrochemical refinery and from a municipal water treatment plant where humidity is as high as 70% with known airborne volatile organic compounds. The results obtained showed excellent sensitivity and selectivity for BCME using the analytical approach described. A precision study was conducted with standards at two different concentrations, 25 μL L^{-1} and 250 μL L^{-1} BCME in purified air. A relative standard deviation of 5% and 3% was determined at 25 μL L^{-1} and 250 μL L^{-1} respectively (n = 10). The technique was shown to have a detection limit of 2 μL L^{-1} and was found to be linear over a range of up to 500 μL L^{-1} with a correlation coefficient of 0.998.

214 BCME can be selectively and accurately measured without pre-concentration or derivatization in
215 less than 60 s. No known chromatographic interferences were observed for a wide range of
216 common compounds such as alcohols, incomplete combustion of fuels found in air in typical
217 industrial environments. Non-condensing water did not yield chromatographic interference.
218 The analytical system is portable with a total weight of less than 8 kg and the system can be
219 forward deployed for field analysis or used in a laboratory. While the technique was proven to
220 be robust, it is worth noting that well purified transport gas is a must to ensure the performance
221 of the spectrometer is not compromised. Contaminants such as hydrocarbons and carbon dioxide
222 must be removed with commercially available zero air generators or with high performance
223 purifying filters.

224 Attempt to apply this methodology to measure CMME was unsuccessful. **Figure 6** shows
225 topographic plots of CMME in purified lab air from 20 μL L^{-1} to 1.6 mL L^{-1}. The intensity of the
226 spot tentatively identified to be CMME did not change substantially over this concentration
227 range. Further, the GC retention time of the spot in question matched with methanol, also
228 depicted in Figure 6. Since CMME in air is known to hydrolyze rapidly to hydrochloric acid,
229 formaldehyde and methanol, it is plausible that the analytical system detected the hydrolyzed
230 product of CMME instead of CMME itself [1]. In any case, the use of this method for the direct
231 measurement of CMME is contra-indicated.

232 A comparative study was carried out involving connecting the μGC to an Agilent ^{63}Ni ECD as
233 the detector is inherently sensitive to halogenated compounds and taking advantage of the fact
234 that BCME has two chlorine atoms. The low power consumption attribute of the detector makes
235 it suitable for use with the μGC even though further form factor development will be required to
236 incorporate the detector into the platform if the feasibility study was successful. The result from

237 the feasibility study showed that due to the excessive void volume in the detector and
238 connections, substantial peak broadening was observed. Moreover, overlapping peaks from
239 oxygenated compounds like isopropanol, degreaser like 1,1,1-trichloroethane, and aromatic
240 compounds like benzene and alkyl benzenes from incomplete combustion process were
241 observed. As a consequence, the option of using μGC-ECD was dismissed.

242

4. CONCLUSIONS:

Direct measurement of part-per-billion level of BCME in air was achieved by using a micromachined differential ion mobility spectrometer hyphenated to a fast gas chromatographic method based on temperature-programmable silicon micromachined technology. No pre-concentration or derivatization was required for the target compound. A complete analysis can be conducted in less than 60 s with a relative precision of less than 5% over a range from 10 μL L^{-1} to 500 μL $L^{-1}$and a detection limit of 2 μL $L^{-1}$with no observable chromatographic interferences. The μGC-DMS was found to be reliable and can be field deployable.

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Figure Legends:

Figure 1: Dispersion Plot of outdoor air from a local park

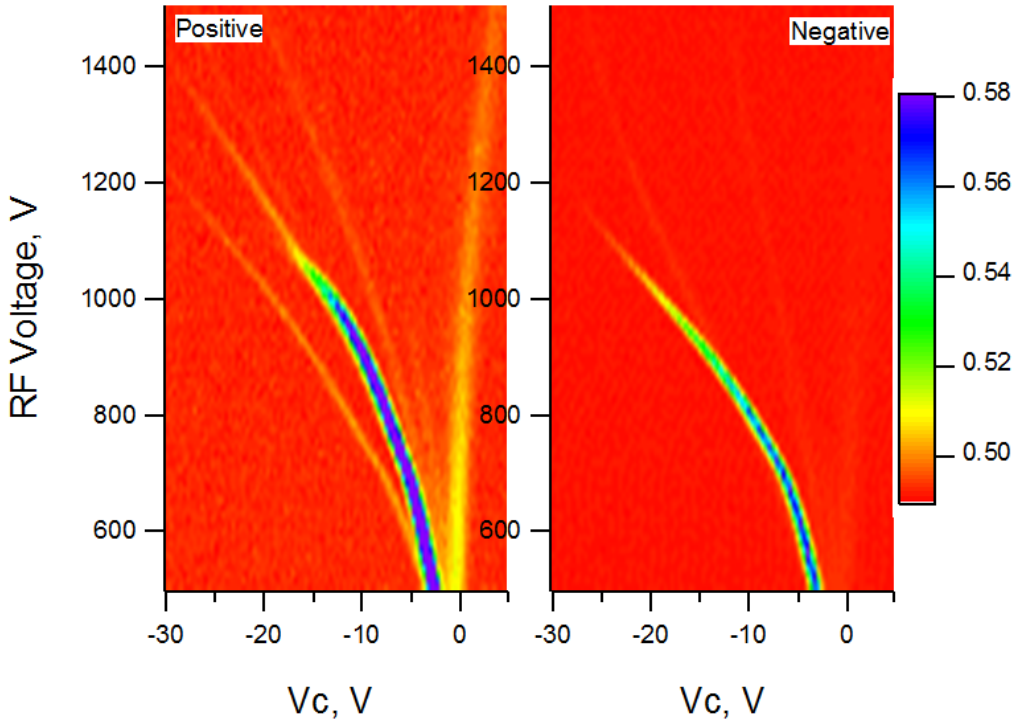
Figure 2: Dispersion plot of 15 mL L^{-1} BCME in purified lab air

Figure 3: Topographic plot of 1 mL L^{-1} BCME in purified lab air

Figure 4: Topographic plots of purified lab air, 50 μL L^{-1}, 1.5 mL L^{-1}, and 7 mL L^{-1} of BCME spiked into air obtained from a local industrial area.

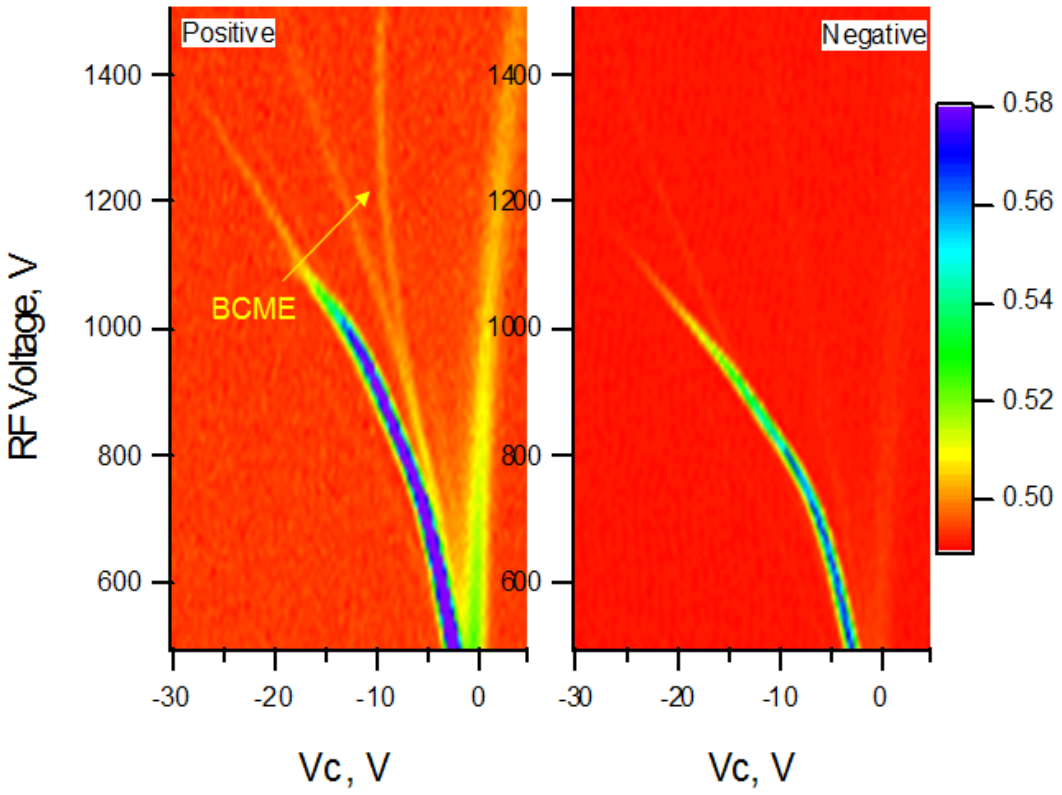
Figure 5a: Chromatogram of 2 μL L^{-1} BCME spiked into a local refinery plant air; 5b Chromatogram of 5 μL L^{-1} BCME spiked into a local municipality water treatment plant air.

Figure 6: Topographic plots of various concentrations of CMME and methanol in purified lab air.


Positive
Negative
RF Voltage, V
1400
1200
1000
800
600
-30
-20
-10
0
Vc, V
0.58
0.56
0.54
0.52
0.50

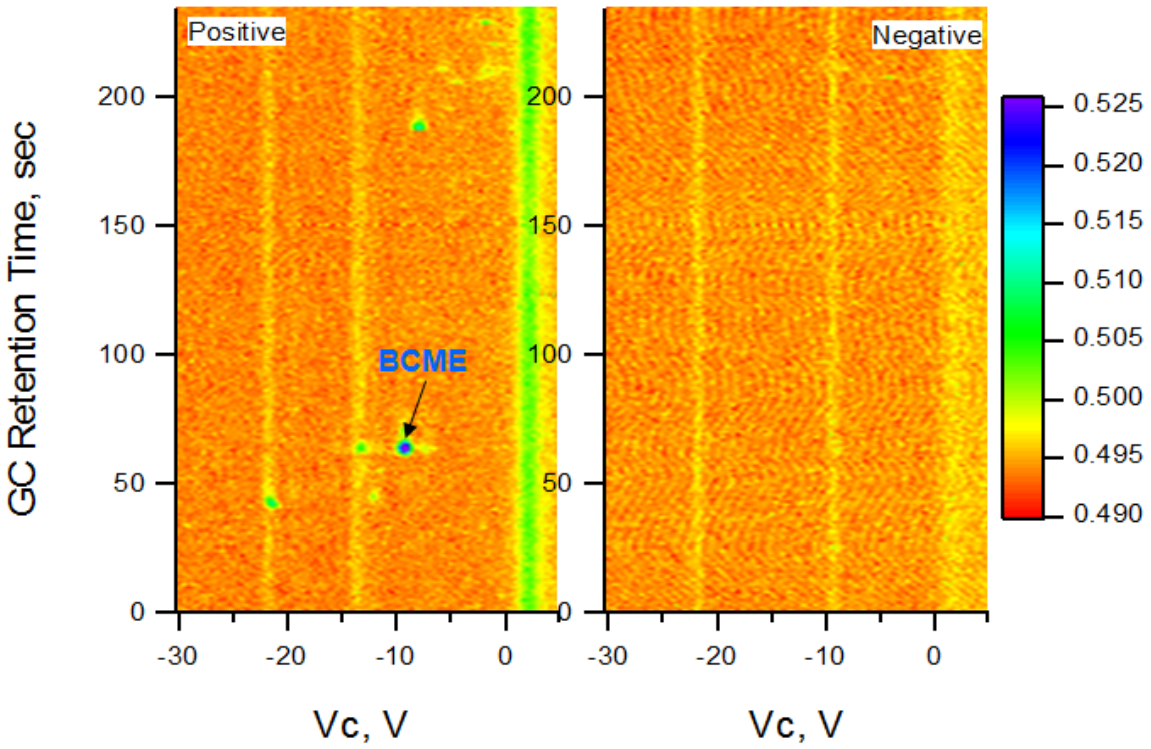
297

298


Positive
Negative
BCME
RF Voltage, V
1400
1200
1000
800
600
-30
-20
-10
0
Vc, V
0.58
0.56
0.54
0.52
0.50

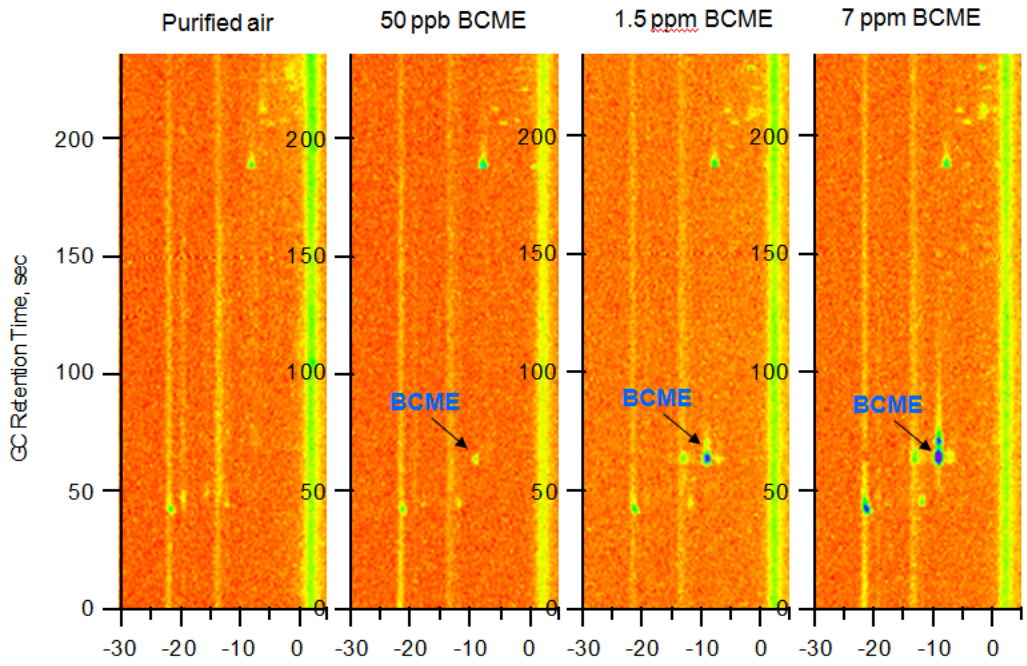
299

300


Positive
Negative
BCME
GC Retention Time, sec
Vc, V
Vc, V
0
50
100
150
200
-30
-20
-10
0
0.525
0.520
0.515
0.510
0.505
0.500
0.495
0.490

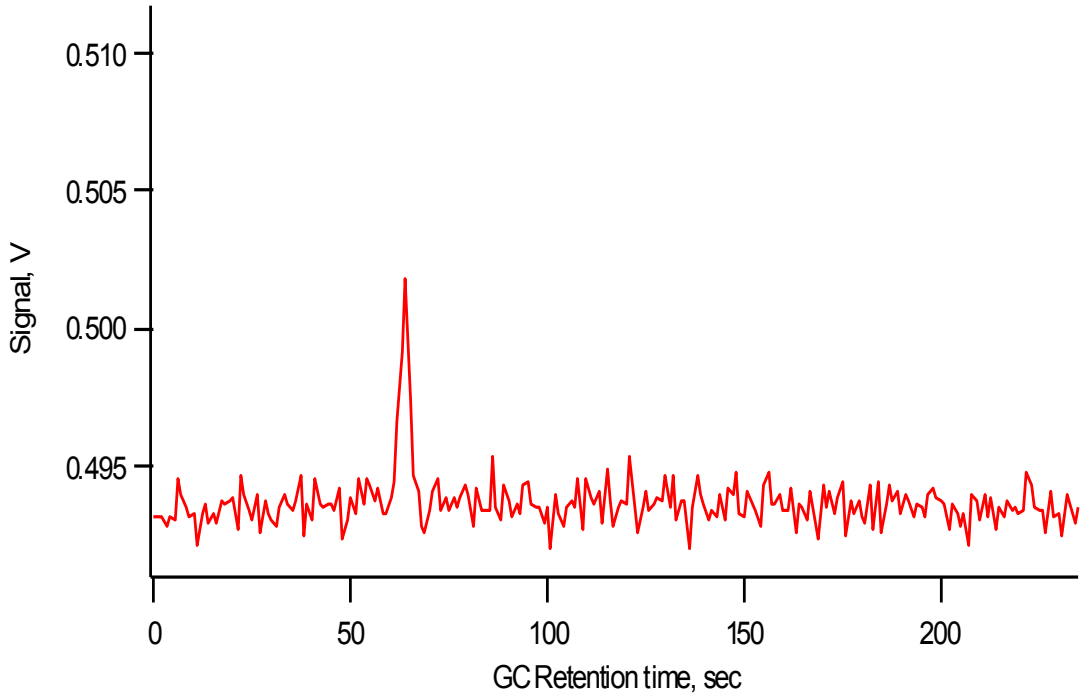
301

302

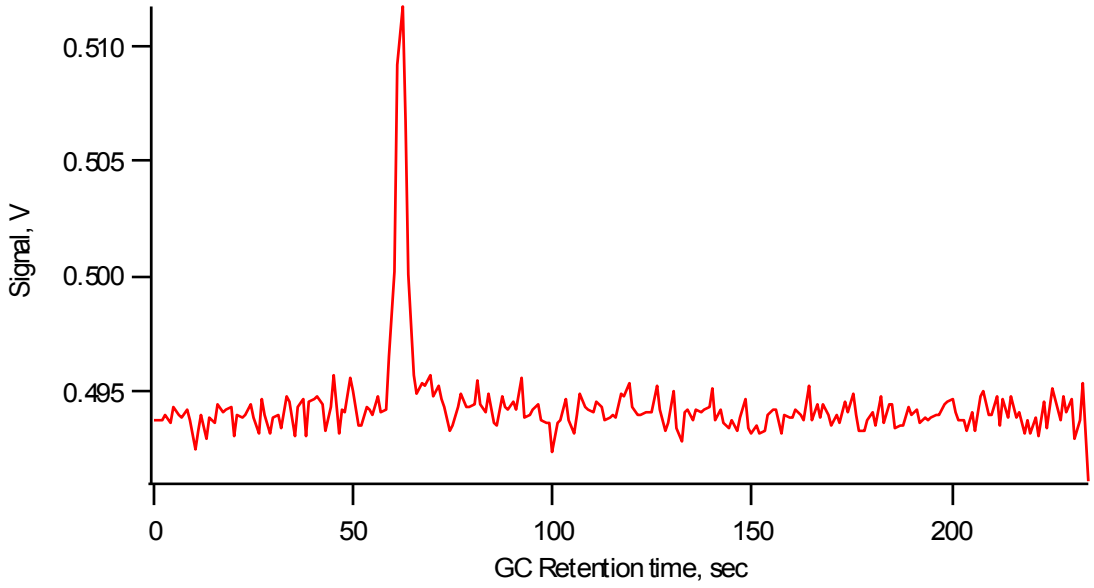

Purified air
50 ppb BCME
1.5 ppm BCME
7 ppm BCME
GC Retention Time, sec
200
150
100
50
0
-30
-20
-10
0
BCME
BCME
BCME

303

304

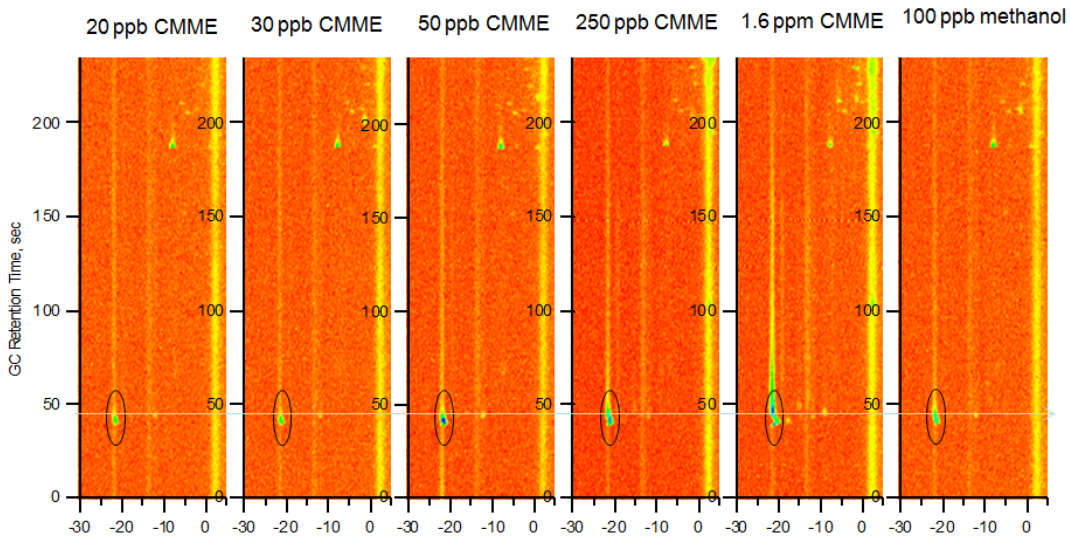

0.510
0.505
0.500
0.495
Signal, V
0
50
100
150
200
GC Retention time, sec

305


0.510
0.505
0.500
0.495
Signal, V
0
50
100
150
200
GC Retention time, sec

306

307


20 ppb CMME
30 ppb CMME
50 ppb CMME
250 ppb CMME
1.6 ppm CMME
100 ppb methanol
GC Retention Time, sec
200
150
100
50
0
-30
-20
-10
0

308

5. Novel Techniques to Solve Difficult Analytical Problems in Gas Chromatography

5.1 Ultra-trace level analysis of morpholine, cyclohexylamine, and diethylaminoethanol in steam condensate by gas chromatography with multi-mode inlet, and flame ionization detection

Chapter 5.1 showcases a novel and reliable analytical approach for a well-known, yet demanding analysis to be conducted by GC - the characterization of amine-based anti-corrosion agents such as morpholine (CAS 110-91-8), cyclohexylamine (CAS 108-91-8), and diethylaminoethanol (CAS 100-37-8) in steam condensate. The compounds cited are often added to the steam condensate as part of a strategy to control corrosion in the water treatment process. This treatment process is employed extensively in industries from conventional and nuclear power generation plants where large quantity of water is processed on a daily basis to the local acute care medical facilities. The stability and great solubility of these compounds in water often result in inadvertent addition to other process streams or final products like potable water. Therefore, close monitoring is necessary. The ability to analyze these compounds in water has historically been difficult, particularly at the ppb level. The analytical technique developed does not require any sample enrichment or derivatization. The technique employs a recently commercialized multi-mode inlet capable of attaining a heating rate of 900 ^{o}C/min. The inlet was operated in pulsed splitless mode with programmed inlet temperature. The strategy involves using a relatively cold temperature at first to transfer the binary solvent matrix without causing large expansion of vapour volume that can overload the liner capacity, then rapidly heating the inlet to the desired temperature to completely vaporize and transfer the analytes. A newly

commercialized base-deactivated capillary column was employed followed by flame ionization detection. A detection limit of 100 ppb_v for all analytes was attained with a complete analysis time of less than 10 minutes.

5.2 Direct measurement of part-per-billion levels of dimethyl sulfoxide in water by gas chromatography with stacked injection and chemiluminescence detection

In ***Chapter 5.2***, a recently innovated sample enrichment technique called stacked injection in combination with a sulfur chemiluminescence detector (SCD) was successfully employed for the characterization of ultra-trace levels of dimethyl sulfoxide (CAS 67-68-5) (DMSO) in water. The use of the stacked injection technique can enhance signal detectability of the analyte of interest by more than one order of magnitude. DMSO is a chemical of industrial significance with many important applications, such as a solvent in chemical reactions involving nucleophilic reactions and salts. It is used extensively as a safer paint stripper when compared to dichloromethane, as a cleaner in the manufacturing of electronics such as flat panel displays, in drug delivery, and medical care-related applications.

Detecting DMSO in water by direct measurement is a significant analytical challenge. Other analytical techniques such as liquid-liquid extraction, headspace or purge-and-trap are ineffective due to the fact that DMSO is completely miscible in water. Reaction gas chromatography, where DMSO is reduced to dimethyl sulfide was found to be inefficient and labour intensive.

When combined with a highly sensitive and selective detector such as the SCD and with stacked injection, where the mass of analyte can be enriched up to one order of magnitude, a detection limit of 2 ppb_v of DMSO can be attained. The analytical approach was successfully implemented with a high degree of reliability.

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6. Future Work

Additional research that can extend the work described in this thesis include the use of planar microfluidic devices for other unique applications in gas chromatography such as:

a) A cryogenic trap to improve the quality of chromatography obtained, especially with ancillary chromatographic devices like a headspace, thermal desorber, or purge-and-trap analyzer where mitigating peak broadening is still a challenge to overcome.
b) As a fast injection device for high speed gas chromatography where a narrow solute bandwidth is required.
c) For targeted signal enhancement to improve signal detectability of an analytical system.
d) For analyte enrichment or field sampling by coating the device with an appropriate trapping material like polydimethylsiloxane.
e) For more than one stream switching like in a "Double Deans Switch" configuration, as well as in comprehensive two dimensional gas chromatography where planar microfluidic devices can be configured as a novel reserved-flow differential flow modulator.

Advances in planar microfluidics will lead to more useful and capable devices that will further improve the performance of gas chromatography both tactically and strategically in the coming years. The chromatographic applications to be developed based on planar microfluidics devices are only limited by the imagination of the researchers.

The need for a highly sensitive and tuneable selective detector will continue to drive the development of differential ion mobility spectrometry. Further research can be made to improve the performance, reliability and portability of the current technology include:

a) Modifying and augmenting DMS separations through vapor dopants.
b) A reliable and clean on-board recirculation system to either reduce or completely eliminate the need for transport gas. Currently, for optimal system performance, a transport gas flow rate of approximately 500 mL/min is required.
c) An alternative, reliable ionization source to Ni^{63} for the spectrometer. In many regions of the world, Ni^{63} is still being closely regulated as it is a radioactive source. As a result, the handling and deployment of the instrument can be quite complicated.
d) The development of a portable DMS-MS or DMS-IMS analytical system capable of performing ultra-trace analysis in complex matrices without the requirement of sample preparation. In this role, DMS can act as a highly effective ion species pre-filter which will improve the overall analytical system sensitivity and selectivity. The unit should be suitable for field deployment as the current trend in analytical measurements suggests a strong bias towards field measurement over remote laboratories.

Three dimensional separations such as GC-GC-DMS, GC×GC-DMS, GC-DMS-DMS, or GC-DMS-MS are worth investigating to offer both improved selectivity and sensitivity for target compounds in the ever increasing complex sample matrices and for throughput enhancements.

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